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Original Article

Ethanol Extract Dry Syrup Granulation Formulation Dayak Onion Bulb (*Eleutherine bulbosa* (Mill.) Urb.)

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Abstract

Background: Dayak onion (*Eleutherine bulbosa* (Mill.) Urb.) is one kind of medicinal plant native to East Kalimantan that has antioxidant activity. The dosage form that can be developed is dry syrup granules which become one of the most simple dosage forms in preparation, easy to use, storage-stable and can cover the bitter taste of the drug. The goal of this study was to find the best mix of Avicel PH 101 and Na CMC to make dry syrup granules that meet the requirements for physical properties. **Methods:** Research was carried out experimentally using three formulas with combinations of Avicel PH 101 and Na-CMC. The ratios of Avicel PH 101 and Na-CMC were (1:0); (0.5:0.5) and (0:1). The evaluation of dry syrup granules included organoleptic observations, a moisture content test, a flowability test, a reconstitution time test, pH test, viscosity test and a hygroscopic test. **Result:** dry syrup granules with variation 1:0 of Avicel PH 101 and Na-CMC have the best requirements for physical properties, i.e. moisture content of 2.47%, the flow time of 0.91 seconds, an angle of repose 25.19 ° and tap index of 10.67%. **Conclusion:** Dry syrup granules with a ratio of Avicel PH 101 and Na CMC (1:0) are preparations that best meet the physical properties requirements, namely moisture content of 2.47%, flow time of 0.91 seconds, angle of repose 25, 19° and a fixing index of 10.67%.

Keywords: - *Dry syrup granules, dayak onion extract, Avicel PH 101, Na-CMC*

Introduction

Dayak onion is a plant commonly found in the Kalimantan region (Zakaria, 2023). The community uses dayak onion bulbs widely as traditional medicine. The chemical compounds contained in Dayak onions include 15 compounds, including flavonoid and naphthaquinone derivatives. Several studies have shown extract activity as anti-inflammatory, antidiabetic, anticancer, antidiabetic, and antimicrobial (Prayitno & Mukti, 2020; Ahmad *et al*, 2023; Kamarudin, 2022). Empirically, the Dayak community has used this plant as a medicine for acne and boils by applying it to pimples or boils after being pounded and mashed (Syamsul *et al.*, 2020). In addition, Dayak onions have also been used in the treatment of various types of diseases such as diabetes mellitus, coronary heart disease, hypertension, hepatitis, tuberculosis, bronchitis, sinusitis, inflammation of the rectum, gout, rheumatism, nephrolithiasis, urinary tract infections, inflammation of the prostate, goiter, ulcers, flatulence, hemorrhoids, obesity, menstrual pain, skin health and sexual disorders (Luh, 2013; Da Silva, 2024; Habibah, 2023). Forest onion (*Eleutherine bulbosa* Mill. Urb) is a plant that has antioxidant activity (Munaeni, 2019). Chemical compounds with strong antioxidants found in forest

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onions are phenolics, flavonoids and tannins, which are suitable for counteracting free radicals (Sharon *et al.*, 2013; Harlita, 2018).

Antioxidant components have an important role in the protection of body health. Experts argue that antioxidants can reduce the risk of chronic diseases like cancer and heart disease. The use of natural antioxidants is currently considered safer because natural antioxidants are obtained from plant extracts. The development of finished dosage forms from efficacious plant extracts will facilitate the public in obtaining the efficacy of these plants. One preparation that can be developed for the community is dry syrup granules. Dry syrup granules are a practical and easy preparation, namely in the form of dry granules, which must be added to a certain amount of water before consumption. Because they can cover up the drug's bitter taste, dry syrup preparations in the form of granules are more storage-resistant and popular with the general public. Dry syrup formula requires a suspending agent in its manufacture to increase the viscosity and produce good physical properties. The combination of Avicel PH 101 and Na CMC is a suspending agent commonly used to manufacture dry syrup (Ofner *et al.*, 1989). The advantage of using Avicel PH 101 is that it can provide excellent stability and maintain the viscosity of the preparation. Avicel PH 101 can also function as a binder, adsorbent, or water absorbent so that a good and stable dry syrup granule preparation can be produced. Na CMC is another suspending agent that is known to have stabilizing properties that help keep the preparation stable and help Avicel PH 101 spread out in the preparation.

Material and Methods

The Tools

The tools were glassware (Pyrex®), an analytical balance (Excellent®), porcelain cup, universal pH paper, knife, blender, No. Mesh sieve. 14 and No. 16, oven (Memmert®), water bath, glass jar, glass funnel.

Materials

Dayak onion bulbs, Na-CMC (Brataco Chemical, pharmaceutical), Avicel PH 101 (Asahi Chemical, pharmaceutical), aspartame, lactose (Brataco Chemical, pharmaceutical), sucrose (Brataco Chemical, pharmaceutical), and tween 80 (Brataco Chemical, pharmaceutical).

Extraction (Maceration)

By soaking the dry simplicia powder in the solvent liquid, it was possible to extract Dayak onion bulbs. Three hundred grams of dry simplicia powder with a suitable degree of fineness were put into a glass container, poured with 3 liters of solvent liquid (70% ethanol), closed and stirred continuously for 6 hours. The simplicia powder that has been stirred is left in the solvent for 18 hours. The juice is sprinkled, and the dregs are squeezed. The same extraction was carried out again using 300 grams of new simplicia powder until a total of all extracts was obtained. The Dayak onion bulb extract was used to identify chemical compound groups. This was done by testing it for alkaloids, flavonoids, phenolics, tannins, steroids, and saponins.

Formulation of Dayak Onion Extract Dry Syrup Granules

The dry syrup granules of Dayak onion ethanol extract are prepared in three formulas, as shown in Table 1. All ingredients used are weighted according to the calculation of the thick extract formula, put into a container, and set aside. Avicel PH 101 and Na-CMC were mixed with tween 80 first, and some lactose was added until well mixed. Little by little, the mixture is put into a container containing the thick extract and stirred thoroughly. Flavour, aspartame, and remaining lactose are added to the thick extract mixture. Dissolved sucrose is added little by little until a lumpy mass is obtained. The mass is passed through a Mesh sieve. The granule mass is dried in an oven at 50°C for 16 hours. The dry granules were weighed and sieved using a No. 16.

Ethanol extract from Dayak onion is formulated for dry syrup granules by using combination of avicel pH 101 and Na-CMC. Therefore, there are 3 types of formulas, each with a different amount of ratio.

The 1:0 ratio of avicel pH 101 and Na-CMC used on "formula I". For "formula II" we used 0,5:0,5 ratio on both substances. Lastly we also used a ratio of 0:1 of avicel pH 101 and Na-CMC for "formula III".

Table 1. Formulation of Dayak Onion Ethanol Extract Dry Syrup Granules

Ingredient	Formulas (g)		
	I	II	III
Dayak Onion Ethanol Extract	0.25	0.25	0.25
Avicel pH 101	1	0.5	0
Na CMC	0	0.5	1
Tween-80	0.1	0.1	0.1
Aspartame	0.5	0.5	0.5
Fragrance	2	2	2
Sucrose	75	75	75
Lactose	21.15	21.15	21.15

Preparation Evaluation

Evaluation of dry syrup granules includes organoleptic observation, moisture content test, flow time test, angle of repose test, determination index and hygroscopic test.

Results and Discussion

Avicel PH 101 and Na-CMC were used in different amounts to make dry syrup granules from the thick extract of Dayak onions. Other additives are tween 80, aspartame, sucrose, lactose, and flavours. As suspending agents, Avicel PH 101 and Na-CMC were picked because these two ingredients are often mixed to make dry syrup granules (Harahap, 2023). In this formulation, Avicel PH 101, apart from being used as a suspending agent, can also be used as a granule binder. The binder can be added in dry form or in solution form (more effective). Two kinds of Avicel are widely used, namely Avicel PH 101, which is in the form of powder, and Avicel PH 102, which is in the form of granules and has a larger size. Avicel PH 101 can speed up the granulation drying process and reduce the risk of over wetting in wet granulation. The method used in this study is the wet granulation method. Making granules begins with preparing all the materials and tools to be used. Mixing all the ingredients is done until a mass that can be clenched is obtained. The mass is passed through a number mesh sieve 14; wet sieving is to obtain granules of the same size and form a more compact granule mass.

The method used in this study is the wet granulation method. Making granules begins with preparing all the materials and tools to be used. Mixing all the ingredients is done until a mass that can be clenched is obtained. The mass is passed through a 14-mesh sieve. The purpose of wet sieving is to obtain granules of the same size and form a more compact granule mass. The wet granule drying process is the process of removing liquid from a substance/material using heat. It is achieved by transferring the liquid from the surface into an unsaturated vapour phase. The drying process will form solid bridges between particles that bind to each other to form granules. Drying the granules too fast at high temperatures will cause the surface of the granules to dry out quickly. The best way to dry the granules is at 40-60°C in a drying cabinet with air circulation and heating control. Granule drying is carried out until the remaining granule moisture content ranges from 2-4%. This residual water is used to reactivate the properties or functions of the binder. The dried granules are passed through a sieve with small holes on the number 16 mesh sieve.

Evaluation of Granule Preparations

Tests include the colour, taste, and aroma of the resulting granules. The organoleptic test results obtained from the three formulas produced the same colour: pale pink. The pale colour produced in the granules is due to the red colour obtained naturally from Dayak onion extract, so bright and attractive colours are not produced. The addition of a fragrance agent during the formulation process results in the three formulas producing an aroma that is distinctive and sweet. For taste testing, the three formulas have a sweet but slightly bitter taste from Dayak onion extract.

Table 2. Data on results of evaluation of dry syrup granules

Parameter	Formulas		
	I	II	III
Moisture Content (%)	2.47	3.73	5.3
Flow Time (sec)	0.91	0.94	1.07
Flow Rate (g/sec)	10.99	10.64	9.34
Point angel (^{0})	25.19	27.02	28.32
Tapping Index (%)	10.67	17.33	20.67

The results obtained from testing the moisture content of the three formulas are shown in Table 2. Based on the three formulas, the first and second formulas produce granule moisture content ranging from 2.47 to 3.73%; this value fulfils the requirements of a good granule moisture content. The third formula produced a granule moisture content of 5.3%; this value did not meet the requirements for a good granule moisture content. Based on the study's results, using Avicel PH 101 affected the absorption of water content. The greater the number of Avicel PH 101 components used, the lower the moisture content of the granules. This is because Avicel PH 101, apart from being used as a suspending agent, also has properties as an adsorbent or absorbs water contained in the granules. Avicel 101 is able to hold or bind 50% of the active substance or have good binding properties (Supomo, 2015). Based on this, the greater the number of Avicel PH 101 components used, the more optimal the absorption of moisture content will be and the more fulfilled the moisture content of the granules will be. This is in line with research by Sa'adah and Fudholi (2011) that found that Avicel pH 101 had the greatest impact on increasing absorption because Avicel can absorb moisture very well, increasing the attractive force between particles.

Na-CMC can also affect the moisture content in the granules because it is hygroscopic, so the greater the Na-CMC, the greater the moisture content of the granules. Na-CMC will be dispersed in water, then hydrophilic Na-CMC grains will absorb water, and swelling will occur. Na-CMC is an anionic polymer that lets more hydrogen bonds form than nonionic cellulose polymers. This means that it sticks to mucosa better (Anil & Sudheer, 2018). This is what causes the second and third formulas to have a higher moisture content when compared to the first formula, which does not contain Na-CMC. The third formula is a preparation that contains Na-CMC with the greatest concentration and does not contain Avicel PH 101 as an adsorbent, so water absorption is not optimal, and the high concentration of Na-CMC in the third formula causes the moisture content to not meet the requirements, namely 2-4%.

Flow time and flow rate are parameters used to determine a material's flow properties. The flow rate is obtained from the time in seconds it takes a certain number of granules to flow through the funnel. The smaller the particle size, the lower the flow rate, so the greater the angle of repose formed. Humidity also has an impact on the flow properties. The higher the humidity, the worse the flow properties of the granules. The flow time test was carried out using 10 grams of granules which were put into a funnel-shaped flow time speed tester, and then the granule flow rate was measured until all the granules flowed out of the test tool. Ten seconds, or the flow rate is greater than 10 grams/second. The smaller the flow time, the better the flow properties and vice versa. If using the flow rate parameter, the greater the flow rate, the better the flow properties. The results obtained from testing the flow time and flow rate of the three formulas are shown in Table 2.

The results show that the first and second formulas meet the flow time requirements. Avicel PH 101 has good flow properties to speed up flow time (Kokafrinsia & Saryanti, 2021). The third formula does not because the first and second formulas have a smaller flow time and a greater flow rate. This can be caused because there are hygroscopic materials, so the granules can absorb moisture from the air, which causes the granules to stick to each other and the funnel. As in the moisture content test, the presence of Na-CMC causes the dry syrup granule preparations to become moister. This situation causes the third formula to have a flow time that does not meet the requirements. The powder is said to have good flow properties if the determination index is less than 20%. The results obtained from

testing the index determination of the three formulas are listed in Table 2. Based on the results of the determination test conducted, the results of the determination index were quite large for the three formulas; the first and second formulas meet the requirements with a determination index of not more than 20%. The third formula must meet the requirements, with a determination index value of 21%. The first formula has the best index value because it has the lowest value compared to the three formulas. The combination of Avicel PH 101 and Na-CMC produces granules with good compressibility. This is because the combination of Avicel PH 101 and Na-CMC is cohesive.

The nature of the flow is determined using the flow slope angle (slope angle, pour angle, glide angle), which results when a powdery substance is allowed to flow freely from the funnel. The powder will form a cone, and then the angle of inclination of the powder will be measured. The flatter the resulting cone, meaning that the angle of inclination of the powder is smaller, the better the flow properties of the powder. The results obtained from testing the angle of repose of the three formulas are shown in Table 3. Based on the data on the angle of repose obtained from the three formulas, all formulas meet the requirements for repose angle, namely granules or powders can flow properly if they have an angle of repose between 25 – 450. The first formula has the best value of the angle of repose compared to the other two formulas, and based on previous test data, the first formula also has the best flow time and moisture content of all formulas. The cohesiveness between the particles affects the angle of repose. The smaller the particle size, the higher the cohesiveness obtained (Elisabeth *et al.*, 2018). This causes the granule to be difficult to flow, and the angle of repose obtained is getting bigger. The water content in the granule preparation can affect the resulting repose angle size. The higher the moisture content of the granules, the higher the frictional forces between particles generated, thus affecting the angle of repose obtained, the greater (Rahayu & Anisah, 2021).

Good dry syrup preparations have certain criteria, which are quickly dispersed homogeneously when suspended. The faster the reconstitution time of a dry syrup preparation, the better the dry syrup preparation will be. The easier it is for a dry syrup to be reconstituted, the easier it will be for patients to use the preparation. Getting a homogeneously dispersed suspension prepared to be drunk does not take much time or effort. The results of the reconstitution time test showed that the greater the Na-CMC content in the preparation, the longer the reconstitution time, and the higher the temperature of the water used to reconstitute the dry syrup, the faster the reconstitution time. The results obtained from testing the reconstitution time of the three formulas are listed in Table 3.

Table 3. Data on Results of Evaluation of Dry Syrup Preparations

Parameter	Formulas		
	I	II	III
Temperature reconstitution time 40ºC (seconds)	29.09	88.29	121.31
Temperature reconstitution time 80ºC (seconds)	22.88	67.67	106.13
Viscosity (poise)	0.036	1,248	0.274
pH (7th day)	6	6	6

The first formula that did not use NaCMC had the fastest reconstitution time of 29 seconds at 40°C and 22 seconds at 80°C. The third formula with the largest amount of NaCMC used had the longest reconstitution time, namely 2 minutes and 1 second at 40°C and 1 minute and 46 seconds at 80°C. The first formula with the fastest reconstitution time is the best in the reconstitution time test, and the third is the formula with the slowest reconstitution time. This is due to NaCMC dispersing in water, then hydrophilic NaCMC grains absorb water, and swelling occurs like lumps. These clumps cause the preparation to be difficult to dissolve. The pH test was carried out to observe changes in pH that occurred at the beginning of the observation (first day) and the end (seventh day). The goal is to determine the degree of acidity and alkalinity of a solution during the storage process (Kusumaningrum, 2020). pH is an important physical parameter that aims to show maximum stability at a specific pH value, and pH fluctuations are undesirable. pH measurement provides fine control over the manufacturing process and product shelf life. A suspension with a high level of acidity (pH) will decrease the viscosity of the suspension liquid, and a suspension with a high level of basicity will increase the viscosity of the liquid.

Based on observations on the first and seventh days, there was no change in pH. This shows that the stability of the suspension is quite good because there is no drastic increase or decrease in the pH value. Suspension preparations require a suspending agent. The suspending agent used in this study was a combination of Avicel PH 101 and Na-CMC, which increased the solution's viscosity. The goal of the viscosity test is to ascertain the suspension's viscosity level after absorption by the body. In addition, the pH level in the suspension has an impact on the preparation's typical viscosity (Hafizah, 2017). With increasing viscosity, it will increase the stability of the suspension solution. When consuming suspension preparations, the patient's comfort depends on the solution's thickness; if the reconstituted suspension is too thick, the patient will find it uncomfortable to drink. The results obtained from testing the viscosity of the three formulas are listed in Table 3. Based on the viscosity test that has been carried out, the results show that the first formula has the smallest suspension viscosity value of 0.0360 poise, and the third formula has the highest suspension viscosity value of 0.2740 poise. Na-CMC serves as a thickening agent, intending to form a colloidal dispersion system and increase the viscosity. Na-CMC has a very high ability to bind water, thus increasing the viscosity of the solution. In contrast, Na-CMC grains are hydrophilic, so they will absorb water and eventually swell. The presence of Na-CMC causes suspended particles to be trapped in the system or stay in place and not settle under the influence of gravity.

Conclusion

Dry syrup granules with a ratio of Avicel PH 101 and Na CMC (1:0) are preparations that best meet the physical property requirements, namely moisture content of 2.47%, flow time of 0.91 seconds, an angle of repose 25- 19° and a fixing index of 10.67%.

Conflict of Interest

The authors declare that there is no conflict of interest.

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References

Ahmad, I., Narsa, A. C., Ramadhani, M. R., Zamruddin, N. M., Iswahyudi, I., Hajrah, H., Indriyanti, N., Arifuddin, M., Siska, S., Supandi, S., & Ambarwati, N. S. S. (2023). Optimization of microwave-assisted extraction on polyphenol metabolite from *Eleutherine bulbosa* (Mill.) urb. bulbs using response surface methodology. *Journal of Advanced Pharmaceutical Technology & Research*, *14*(2), 113–118. https://doi.org/10.4103/japtr.japtr_613_22

Anil, A., & Sudheer, P. (2018). Mucoadhesive Polimers: A. Review. *Journal of Pharmaceutical Research*, 17(1), 48-55. https://japsonline.com/admin/php/uploads/209_pdf.pdf.

da Silva, R. M. G., Alves, C. P., Barbosa, F. C., Santos, H. H., Adão, K. M., Granero, F. O., ... & Silva, L. P. (2024). Antioxidant, antitumoral, antimetastatic effect and inhibition of collagenase enzyme activity of Eleutherine bulbosa (Dayak onion) extract*: In vitro, in vivo* and in silico approaches. *Journal of Ethnopharmacology*, *318*, 117005. https://doi.org/10.1016/j.jep.2023.117005

Elisabeth, V., YamLean, P. V. Y. and Supriati, H. S. (2018). Formulasi Sediaan Granul dengan Bahan Pengikat Pati Kulit Pisang Goroho (*Musa acuminafe* L.) dan Pengaruhnya pada Sifat Fisik Granul. *Jurnal Ilmiah Farmasi*, 7(4): 1–11. https://ejournal.unsrat.ac.id/v3/index.php/pharmacon/article/view/21416.

Hafizah, A., Wardana, D., & Pratiwi, A. (2017). Formulasi Sediaan Suspensi Menggunakan Suspending Agent Dari Biji Salak Pondoh (*Sallaca Zallaca* (Gaertn).Voss) Dan Biji Buah Salak Bali (*Sallaca Zallaca* Ertn) Var. Amboinensis (Becc) Mogea. *Jurnal Ilmu Kesehatan Dan Farmasi*, *5*(2), 43-48. https://doi.org/10.51673/jikf.v5i2.551.

Habibah, N. A., Lutfiah, A., Liana, A., Tunjung, W. A. S., Indrowati, M., & Pa'ee, F. (2023). Callogenesis of Dayak Onion (*Eleutherine palmifolia*) Bulb in response of Picloram, 2, 4-D, and Kinetin. *Biosaintifika: Journal of Biology & Biology Education*, *15*(2), 270-280. https://doi.org/10.15294/biosaintifika.v15i2.46501

Harahap, H. Y., Futri, C. L., Aminah, D., & Tri, W. (2023). Dayak Onion Tuber (Eleutherine Bulbosa (Mill)(Urb) Extract Ethanol Test on The Histopatological Description of Pancreas Wistar Rat Inducted Streptozotocin. *KnE Social Sciences*, 772-780. https://doi.org/10.18502/kss.v8i4.12972

Harlita, T. D., Oedjijono, & Asnani, A. (2018). The Antibacterial Activity of Dayak Onion (*Eleutherine palmifolia* (L.) Merr) towards Pathogenic Bacteria. *Tropical Life Sciences Research*, *29*(2), 39–52. https://doi.org/10.21315/tlsr2018.29.2.4

Kamarudin, A. A., Sayuti, N. H., Saad, N., Razak, N. A. A., & Esa, N. M. (2022). Induction of apoptosis by *Eleutherine bulbosa* (Mill.) Urb. bulb extracted under optimised extraction condition on human retinoblastoma cancer cells (WERI-Rb-1). *Journal of Ethnopharmacology*, *284*, 114770. https://doi.org/10.1016/j.jep.2021.114770

Kokafrinsia, Z. T. and Saryanti, D. (2021). Optimasi Campuran Avicel PH 101 dan Laktosa sebagai Bahan Pengisi pada Tablet Ekstrak Bunga Rosella (*Hibiscus sabdariffa* L.) Secara Granulasi Basah. *Jurnal Riset Kefarmasian Indonesia*, 3(2):102–116. https://doi.org/10.33759/jrki.v3i2.124.

Kusumaningrum, ID.,Wardani, CC. (2020). Pengaruh konsentrasi Natrii Carboxymethylcellulosum (CMC Na) sebagai suspending agent terhadap stabilitas fisik pada sediaan suspensi kloramfenikoL. *Pharmaceutical and Traditional Medicine*, *1*(2), 84-89. http://www.lppm.poltekmfh.ac.id/index.php/ptm/article/view/77.

Luh, Ni Indrawati dan Razimin. (2013). Bawang Dayak Si Umbi Ajaib Penakluk Aneka Penyakit. Agromedia Pustaka: Jakarta.

Munaeni, W., Yuhana, M., Setiawati, M., & Wahyudi, A. T. (2019). Phytochemical analysis and antibacterial activities of *Eleutherine bulbosa* (Mill.) Urb. extract against Vibrio parahaemolyticus. *Asian Pacific Journal of Tropical Biomedicine*, *9*(9), 397-404. *https://doi.org/*10.4103/2221-1691.267669

Ofner III, C. M., Schnaare, R. L., dan Schwartz, J.B. (1989). *Pharmaceutical Suspensions*. Di dalam: Lieberman H.A., Rieger,M. M., dan Banker, G. S. (eds.) Pharmaceutical Dosage Forms: Disperse Systems. Vol 2. Marcel Dekker, Inc: New York. page: 243-258.

Prayitno, M. and Mukti, BH. (2020). Optimasi Potensi Bawang Dayak (*Eleutherine* Sp.) Sebagai Bahan Obat Alternatif. *Jurnal Pendidikan Hayati*. 4(3): 149-158. https://jurnal.stkipbjm.ac.id/index.php/JPH/article/view/436/231.

Rahayu, S. and Anisah, N. (2021). Pengaruh Variasi Konsentrasi Amprotab Sebagai Desintegrant Terhadap Sifat Fisik Tablet Ekstrak Buah Pare (*Momordica charantia* L.). *Jurnal Ilmiah Ibnu Sina (JIIS): Ilmu Farmasi dan Kesehatan*. 6(1): 39–48. https://doi.org/10.36387/jiis.v6i1.572.

Sa'adah, H., Fudholi, A. (2011). Optimization of Theophylline Tablet Formula Using CoProcessed Excipients of Lactose and Avicel. *Majalah Farmasi Indonesia*. 22(4): 306-314. https://indonesianjpharm.farmasi.ugm.ac.id/index.php/3/article/view/648.

Sharon.N, Anam.S, Yuliet. (2013). Formlasi Krim Anitioksidan Ekstrak Etanol Bawang Hutan (*Eleutherine palmifolia* L. Merr). *Online Jurnal of Natural Science*. 2(3) : 111-122. http://jurnal.untad.ac.id/jurnal/index.php/ejurnalfmipa/article/view/1872.

Supomo, S., Bella R.W, D., & Sa'adah, H. (2015). Formulasi Granul Ekstrak Kulit Buah Manggis (*Garcinia mangostana*. L) Menggunakan Aerosil dan Avicel PH 101. *Journal of Tropical Pharmacy and Chemistry*, *3*(2), 131–137. https://doi.org/10.25026/jtpc.v3i2.99.

Syamsul, E., Supomo, S., Wijaya, H., & Nugroho, B. (2020). Ethanolic Extract Formulation Of Bawang Tiwai (*Eleutherine americana*) In Antiacne Cream. *Majalah Obat Tradisional, 20*(3), 149-157. http://dx.doi.org/10.22146/tradmedj.8860*/ doi:https://doi.org/10.22146/tradmedj.8860

Zakaria, N. H., Saad, N., Che Abdullah, C. A., & Mohd Esa, N. (2023). The Antiproliferative Effect of Chloroform Fraction of *Eleutherine bulbosa* (Mill.) Urb. on 2D- and 3D-Human Lung Cancer Cells (A549) Model. *Pharmaceuticals (Basel, Switzerland)*, *16*(7), 936. https://doi.org/10.3390/ph16070936